NIH launches discussion of *in utero* gene therapy...

[WASHINGTON] The US National Institutes of Health (NIH) last week started what promises to be a prolonged and thorny discussion about the desirability of embarking on *in utero* gene therapy, a move that critics argue threatens to open up a "slippery slope to eugenics" (see *Nature* **395**, 309; 1998).

After meeting for two days, NIH's Recombinant DNA Advisory Committee (RAC) announced a plan to set up four working groups to discuss various aspects of two newly proposed experiments, from informed consent — a clear difficulty when the subject is unborn — to issues of research design.

Following a broader 'gene therapy policy conference' on *in utero* therapy next January, the RAC will modify its guidelines, untouched since 1990, to address the issue.

The meeting focused on the dangers and merits of proposals brought to the RAC by W. French Anderson, professor of biochemistry and paediatrics at the University of Southern California, who has pioneered gene therapy in humans. Anderson and his collaborator, Esmail Zanjani of the University of Nevada School of Medicine, in Reno, are proposing two treatments for fetuses.

One treatment is for α-thalassaemia, an error of haemoglobin manufacture that in its severest form kills in the womb. Fetal blood would be withdrawn and incubated with a virus bearing the healthy form of the gene that otherwise causes production of abnormal haemoglobin. The cells would then be reinjected in the hope that they would produce normal haemoglobin.

The other treatment is for severe combined immunodeficiency (SCID), caused by a lack of the enzyme adenosine deaminase. Sufferers face immediate risk of succumbing to infection after birth. A retrovirus bearing the normal gene for adenosine deaminase would be injected into the peritoneal cavity of the developing fetus in the hope that it will be taken up by fetal immune-system cells.

Gene therapy in the fetus is thought to increase the chance of successful gene integration because cells divide much more rapidly than in adults. But it poses various risks, from altering germ cells to introducing harmful mutations in wrongly targeted cells.

A further risk is that the treatment would bring about only a partial cure, which some meeting participants argued could be worse for children with α-thalassaemia than if they had been left to die prenatally.

There are also concerns about risks of the therapies to mothers. For instance, toxic side effects to the mother in untreated α-thalassaemia are so severe that fetuses are aborted even before they die spontaneously. Some RAC members suggested that prolonging fetal life with experimental treatment may not be justifiable.

Anderson said he brought the proposals to RAC to raise "the issue of a potential inadvertent germline gene transfer", among other risks. "If it is not possible to reduce those risks to an acceptable level [in the estimation of the Food and Drug Administration (FDA) and the NIH] we will not go forward," he said.

Claudia Mickelson, chair of RAC and the biosafety officer at the Massachusetts Institute of Technology, emphasized that the proposals were taken up for "public discussion" purposes only.

But Amy Patterson, an FDA official who this month becomes director of NIH's Office of Recombinant DNA Activities, said that, once RAC develops its policy, the FDA would need a "very compelling" reason to ignore RAC's recommendations. **Meredith Wadman**

...and seeks to repair 'flaw' in review process

[WASHINGTON] The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) intend to repair a "flaw" in the system under which gene therapy experiments are approved, NIH officials announced last week.

Last year, the authority of the NIH's Recombinant DNA Advisory Committee (RAC) to approve or disapprove gene therapy experiments was shifted to the FDA. But RAC was meant to advise the FDA on new proposals.

But RAC chair Claudia Mickelson says that protocols have been approved by the FDA before RAC, which meets only quarterly, has had a chance to comment.

Lana Skirboll, NIH's associate director for science policy, says the NIH now plans to guarantee "full public discussion of all novel gene therapy protocols before any patient is treated".

She adds that FDA and NIH are "in full agreement" that RAC's lack of chances to provide input "is frankly a flaw in the system". Details of the new procedure are expected to be announced in January.

The Senate Appropriations Committee last month adopted language attached to a 1999 spending bill, which "strongly" encourages NIH director Harol Varmus to restore RAC's power to approve or disapprove all human gene therapy experiments. **M.W.**

Canadian research councils publish joint code on ethics

[MONTREAL] **Canada's three major research fund-granting councils have published what they claim is the first broad-ranging ethics policy statement produced for research involving humans in all academic disciplines.**

The statement is aimed at ensuring that research subjects will be treated with respect and privacy; that researchers and their institutions will know their work meets ethical standards; and that Canadian society will benefit from research conducted in a socially and scientifically responsible manner.

It results from several years of discussion, consultation and consensus-building among Canadian academic researchers in the humanities, social and natural sciences, medicine and engineering.

The Medical Research Council, the Natural Sciences and Engineering Research Council and the Social Sciences and Humanities Research Council have had separate ethics policies for 20 years, but this is their first joint document. All researchers and institutions receiving their grants will have to adhere to it.

Some 350 research ethics boards in universities, hospitals and research institutes across the country review proposals for research involving humans, with authority to approve or reject proposals. The new code will update their guidelines.

A news release said the policy statement "seeks to balance the need to advance knowledge and understanding with the need to respect the existing legal, social and moral principles and responsibilities to those who participate in research as research subjects".

The document deals with consent, privacy and confidentiality; conflicts of interest; exclusion of certain groups; research involving aboriginal peoples; the conduct of clinical trials; human genetic research; and research using human gametes, embryos and fetuses.

The document cites changes in the context of research as reasons for a new approach. These included new research tools, a shift from individuals working alone to teams in centres around the world, and questions of ownership and commercialization.

Recent events have thrust such issues into the public eye. In June, for example, the pharmaceutical company Bristol-Myers Squibb attempted to stop publication of an independent report on cholesterol-lowering drugs by the Canadian Co-ordinating Office for Health Technology Assessment (CCOHTA).

CCOHTA challenged this in court, calling it an issue of freedom of speech. The company said the report was flawed and that it was not trying to stifle free speech, but to ensure that the medical profession had correct information. CCOHTA won the case. **David Spurgeon**